

APPROVED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

R-CIN PLUS coated tablet

Rifampicin and isoniazid

R-CIN PLUS is sugar-free

Read all of this leaflet carefully before you start taking R-CIN PLUS

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- R-CIN PLUS has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What R-CIN PLUS is and what it is used for
2. What you need to know before you take R-CIN PLUS
3. How to take/use R-CIN PLUS
4. Possible side effects
5. How to store R-CIN PLUS
6. Contents of the pack and other information

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1. What R-CIN PLUS is and what it is used for

R-CIN PLUS contains two different medicines called rifampicin and isoniazid. They both belong to a group of medicines called anti-tuberculous medicines. They work by killing the bacteria that cause tuberculosis.

R-CIN PLUS is used for the continuation phase of treatment of tuberculosis (TB) in newly diagnosed patients and for re-treatment cases.

2. What you need to know before you take/use R-CIN PLUS

Do not take R-CIN PLUS:

- if you are hypersensitive (allergic) to rifamycins, isoniazid, or to any of the ingredients of R-CIN PLUS (see section 6)
- if you have jaundice (damaged liver) and acute porphyria (a disease where the body cannot make certain substances in the blood and presents with skin problems and/or affects the nervous system)
- if you suffer from thrombocytopenia (a decrease of platelets in the blood) or purpura (the appearance of red or purple discolorations of the skin)
- if you are taking saquinavir, ritonavir or nevirapine to treat HIV
- if you have alcoholism, liver function disease, kidney failure and get seizures (fits).

Warnings and precautions

Take special care with R-CIN PLUS:

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It is important to note that R-CIN PLUS should not be used as first line treatment or for the prevention of tuberculosis.

Both rifampicin and isoniazid contained in R-CIN PLUS have been associated with liver dysfunction. If you have impaired liver function you should only take R-CIN PLUS if it is necessary, it should be under strict medical supervision and caution should be used. Your healthcare provider will want to check your liver before starting treatment with R-CIN PLUS.

The risk of hepatitis (liver failure) may increase with age, daily consumption of alcohol, when liver disease is already present, intravenous drug abuse and in black or Hispanic women. You should be monitored for signs of hepatitis (liver failure) such as diarrhoea, nausea or vomiting, loss of appetite, fatigue, weakness and malaise (feeling of general discomfort).

Serious skin reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP) have been reported with the use of R-CIN PLUS.

- SJS/TEN can appear initially as reddish target spots or circular patches often with central blisters on the trunk. Ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications or be fatal.

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- DRESS appears initially as flu-like symptoms and a rash on the face then an extended rash with a high body temperature, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes.
- AGEP appears at the initiation of treatment as a red, scaly widespread rash with bumps under the skin and blisters accompanied by fever. The most common location: mainly localised on the skin folds, trunk, and upper extremities.

The highest risk for occurrence of serious skin reactions is within 2 days to 2 months after treatment initiation depending on the condition.

If you develop a serious rash or another of these skin symptoms, stop taking R-CIN PLUS tablets and contact your doctor or seek medical attention immediately.

If you have a rare blood problem called porphyria this condition may, rarely, be made worse by R-CIN PLUS.

If you have a problem with bleeding or a tendency to bruise easily R-CIN PLUS may make this condition worse. Your doctor may prescribe additional vitamin K whilst you are taking this medicine.

If you are diabetic, alcoholic, elderly, malnourished, uraemic (have an excess of urea and other nitrogenous waste in the blood) or pregnant and are at risk of neuropathy (nerve damage resulting in numbness) or pyridoxine deficiency, you should be taking a 10 mg daily pyridoxine supplement.

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If you are diabetic R-CIN PLUS can cause false positive reactions with copper sulphate urine glucose tests.

Contact your doctor immediately:

- If you experience allergic reactions such as itchy skin or swollen throat. It is important not to interrupt your dosage to avoid side effects
- if you experience signs of optic neuritis (inflammation of the nerves in the eye)
- if you feel no improvement within 2 – 3 weeks
- if you experience signs of weakness, numbness or pain, usually in hands and feet)
- if vascular reactions (redness or itching of the skin, hot feeling, rapid or pounding heartbeat, sweating, chills or clammy feeling) occur after eating cheese or fish while on R-CIN PLUS.

R-CIN PLUS may decrease the efficacy of oral contraceptives containing estrogen. Consult your doctor about using another form of birth control during treatment.

R-CIN PLUS can cause urine, faeces, saliva, sputum, sweat and tears to turn reddish orange to reddish brown and may also permanently discolour soft contact lenses. Do not wear soft contact lenses while taking R-CIN PLUS.

Consult your doctor or dentist concerning proper oral hygiene while taking R-CIN PLUS.

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Taking R-CIN PLUS may affect the results of some blood tests, especially tests for folate and vitamin B12. If you are going to take blood tests it is important to tell your doctor that you are taking R-CIN PLUS.

Blood Tests

Your doctor will need to check your blood before you take this medicine. This will help your doctor know if any changes happen to your blood after taking this medicine. If you are aged 35 years or older, you will also need to have monthly blood tests to check how your liver is working.

Other medicines and R-CIN PLUS

Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)

Do not take R-CIN PLUS with the following:

- Saquinavir or ritonavir used for HIV infection (see Do not take)

The following medicines should be taken at different times to R-CIN PLUS:

- Antacids (medicines used for indigestion) that contain aluminium should be taken at least 1 hour after taking R-CIN PLUS.
- Para-aminosalicylic acid (PAS) (to treat TB) and R-CIN PLUS should be taken at least 8 hours apart.

Tell your healthcare professional if you are taking any of the following medicines:

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Heart and blood medicines:

- Antidysrhythmics (medicine used to treat abnormal heart rhythm such as disopyramide, lorcinide, mexiletine, propafenone, quinidine, tocainide and digoxin).
- Beta blockers used for heart problems or to control heartbeat and hypertension (such as metoprolol, propranolol and bisoprolol, enalapril).
- Calcium channel blockers used to lower blood pressure (such as diltiazem, nifedipine, verapamil, nimodipine, isradipine, nicardipine and nisoldipine).
- Clofibrate and statins used to treat high cholesterol.
- Warfarin (used to thin blood).
- Water tablets (diuretics) such as eplerenone.

Mental health, epilepsy and motor neurone medicines:

- Benzodiazepines such as diazepam, triazolam, chlordiazepoxide, flurazepam, prazepam (used to calm and reduce anxiety) and benzodiazepine- related medicines (e.g. zopiclone and zolpidem).
- Antipsychotics such as haloperidol and aripiprazole (medicine used to treat psychosis).
- Antidepressants such as amitriptyline, nortriptyline (medicines used in the treatment of depression).
- Riluzole (used to slow the progress of a disease that causes degeneration of nerve cells in the brain and the spinal cord).
- Phenytoin, carbamazepine, ethosuximide and primidone used for seizures or fits.
- Barbiturates (medicine used to help you sleep, anxiety and fits) such as phenobarbital.

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Medicines for infections and the immune system:

- Antifungals such as ketoconazole, fluconazole, itraconazole, voriconazole used in treatment of fungal infections.
- Antiretroviral medicines such as amprenavir, delavirdine, efavirenz, indinavir, maravir, nelfinavir, nevirapine, ritonavir, saquinavir, atazanavir, lopinavir, zidovudine, stavudine and zalcitabine (used in the management of HIV infection).
- Some medicines used for hepatitis-C viral infections such as daclatasvir, simeprevir, sofosbuvir and telaprevir.
- Antibiotics such as dapsone, chloramphenicol, clarithromycin, clofazimine, cycloserine, doxycycline, fluoroquinolones, telithromycin and trimethoprim (used in treatment of bacterial infections).
- Medicines used for lowering your immune system such as ciclosporin, sirolimus and tacrolimus, bone marrow depressants.
- Praziquantel (used to treat worms).
- Atovaquone - used for pneumonia.

Hormone and cancer medicines:

- Some hormone medicines (anti-estrogens) used for breast cancer or endometriosis such as tamoxifen, toremifene and gestrinone.
- Progestin, estrogen, progestogens, systemic hormones (in contraceptives and hormone replacement therapy).
- Irinotecan - used for cancer.
- Levothyroxine (thyroid hormone) used for thyroid problems.

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- Some medicines used for cancer (cytotoxics) such as imatinib

Pain and inflammation medicines:

- Corticosteroids used for inflammation (such as prednisolone)
- Narcotic analgesics (used as certain painkillers) such as morphine, fentanyl or pethidine
- Paracetamol

Other medicines:

- Methadone (pain reliever or medicine to treat addiction)
- Anaesthetics such as enflurane and alfentanil (medicines used to numb the pain during an operation)
- Medicines used to relax muscles before surgery (anaesthetics) such as halothane
- Oral medicines used for diabetes (high blood sugar) such as tolbutamide, chlorpropamide, glyburide and rosiglitazone
- Aminophylline, oxtriphylline and theophylline used in respiratory disease such as asthma
- Quinine (anti-malaria medication)
- Ondansetron (medicine used for nausea and vomiting)
- Probenecid used in the therapy of gout
- Pyridoxine (Vitamin B6)
- Disulfiram (medicine used in the treatment of chronic alcoholism)
- Clofazimine (used in the treatment of leprosy)

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- Other antibiotic medicines such as cefazolin

R-CIN PLUS with food and drink

R-CIN PLUS must be taken on an empty stomach. Eating cheese, such as mature chesses, red wine, beer or fish, such as tuna, skipjack, mackerel, salmon or sardines/pilchards while taking R-CIN PLUS which contains isoniazid (see What R-CIN PLUS contains) may result in redness or itching of the skin, hot feeling, rapid or pounding heartbeat, sweating, chills or clammy feeling, headache, or light headedness.

Avoid taking alcohol while on R-CIN PLUS.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before using R-CIN PLUS.

The safety of R-CIN PLUS has not been established in pregnancy and lactating women.

R-CIN PLUS passes into mother's milk and you should not breastfeed your baby while taking R-CIN PLUS.

Driving and using machines

R-CIN PLUS may influence your ability to drive as dizziness, drowsiness and vision problems or have other side effects.

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It is not always possible to predict to what extent R-CIN PLUS may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which R-CIN PLUS affects them.

3. How to take/use R-CIN PLUS

Do not share medicines prescribed for you with any other person. Always use R-CIN PLUS exactly as your doctor has told you. You should check with your doctor or pharmacist if you are unsure.

Take R-CIN PLUS tablets with a full glass of water 30 minutes before or 2 hours after meals. If you are taking antacids containing aluminium, use R-CIN PLUS 1 hour after the antacids.

Adults:

The recommended treatment dosages, based on your body weight, for 4 month continuation-phase treatment in adults and children over 12 years of age are as follows as prescribed your doctor (either dosing 5 days a week or daily dosing):

- 30 – 37 kg 2 tablets
- 38 – 54 kg 3 tablets

Children:

R-CIN PLUS is not recommended for children under 12 years.

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Your doctor will tell you how long your treatment with R-CIN PLUS will last. Do not stop treatment early because your TB will not be treated properly.

If you have the impression that the effect of R-CIN PLUS is too strong or too weak, tell your doctor or pharmacist.

If you take/use more R-CIN PLUS than you should

In the event of overdose, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

Symptoms of overdose may include:

- nausea, vomiting, stomach pain, itching, headache, feel tired, sleepy, dizzy, light-headed, have blurred or strange visions (hallucinations), faint or feel faint, seizures, disorientation, slurring of speech, coma, hyperglycaemia, muscle aches, fatigue, frequent urination, thirst, dry mouth. Other signs of taking too much include fast heartbeat, uneven heartbeats, fits and heart attack.

If you forget/use to take R-CIN PLUS

Take the missed dose as soon as you remember. If it is almost time for your next regularly scheduled dose, skip the missed dose and take the next one at the next regularly schedule time.

Do not take a double dose to make up for forgotten individual doses.

If you stop taking/using R-CIN PLUS

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You should only stop taking the tablets if your doctor tells you to. Stopping and starting your treatment could cause unwanted side effects.

4. Possible side effects

R-CIN PLUS can have side effects.

Not all side effects reported for R-CIN PLUS are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using R-CIN PLUS, please consult your healthcare provider for advice.

If any of the following happens, stop using R-CIN PLUS and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to R-CIN PLUS. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- serious skin rashes including Steven-Johnson syndrome, toxic epidermal necrolysis.

These can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms

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- widespread rash, high body temperature, liver enzyme elevations, blood abnormalities (eosinophilia), enlarged lymph nodes and other body organs involvement (Drug Reaction with Eosinophilia and Systemic Symptoms which is also known as DRESS or drug hypersensitivity syndrome)
- a red, scaly widespread rash with bumps under the skin and blisters accompanied by fever at the initiation of treatment (acute generalized exanthematous pustulosis)
- serious blood condition causing bruising and dark red spots under skin which do not go away when you press on them (purpura) or you bruise more easily than usual
- you get more infections more easily than normal with signs including fever, sore throat or mouth ulcers, sores in the throat, bleeding gums, bone pain, low blood pressure, fast heartbeat, and trouble breathing (this could be because you have a low number of white blood cells – leukopenia or agranulocytosis)
- you have severe bleeding (haemorrhage), blood clotting in blood vessels which can cause bleeding
- you have a sudden severe headache. This could be a sign of bleeding in the brain
- severe watery diarrhoea that will not stop and you are feeling weak and have fever (pseudomembranous colitis). You should seek medical attention should this occur.
- severe pain in the stomach through to back (pancreatitis)
- you get confused, sleepy, cold clammy skin, shallow or difficult breathing, a racing heartbeat or your skin is paler than normal (these could be signs of shock)
- blood in your urine or an increase or decrease in amount of urine you produce, difficulty in urinating, swelling, especially of the legs, ankles or feet - this may be caused by serious kidney problems

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- tiredness/listlessness, unusually pale skin colour, shortness of breath (signs of a serious type of anaemia)
- mental disturbances, seizures (fits), coma, subtle personality changes, dementia, memory impairment, delusions, hallucinations (seeing or hearing things that are not there), impulsive decisions, paranoia, anti-social behavior, confusion
- inflammation of the liver (hepatitis) with symptoms including yellowing of the skin or whites of the eyes, or urine getting darker and stools paler, fatigue, weakness, malaise, loss of appetite, nausea or vomiting

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- headache, drowsiness, dizziness, poor coordination, general numbness
- nausea, vomiting, anorexia, abdominal pain, constipation, dry mouth
- permanent staining of soft contact lenses
- increased blood results such as bilirubin, liver enzymes

Less frequent side effects:

- diarrhoea
- eye irritation, vision disturbances
- flu-like symptoms (chills, headache, dizziness, difficulty in breathing, bone pain, fatigue and shivering)
- rash, acne, peeling

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- peripheral neuropathy (damage to nerves outside the spinal cord, affecting the normal functioning of the body's organs and movement and/or feeling of sensation in the extremities, including your arms and legs)
- fever

The following side effects have been reported but the frequency for them to occur is not known:

- influenza
- muscle weakness, cramps, stiffness, spasm
- water retention (oedema) which may cause swollen face, stomach, arms or legs
- decreased appetite, high blood sugar (hyperglycaemia), vitamin D deficiency (with symptoms including inflamed skin, diarrhoea, dementia, and sores in the mouth)
- reddish-orange discolouration of urine, faeces, saliva, sputum, sweat and tears
- flushing, inflammation of blood vessels, bleeding
- difficult or laboured breathing, wheezing
- stomach pains (ulcers) and blood in faeces, tooth discolouration
- skin itching, hives, fluid-filled blisters, painful sores and blisters on your skin and in your mouth (pemphigus), hair loss
- muscle pain or loss of muscle reflexes, bone pain
- heavy bleeding after the birth of your baby, entry of foetal blood into the maternal circulation before or during delivery
- disturbances of menstrual cycle
- you have one of a group of disorders that can cause nerve or skin problems (porphyria) and your condition gets worse

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- low blood pressure, liver test abnormalities
- unusual skin sensations such as feeling numb, tingling, pricking, burning or creeping on the skin (paraesthesia), muscle weakness, loss of tendon reflexes
- balance problems with dizziness (vertigo)
- breast enlargement in men
- blood tests that show autoantibodies that can damage your joints, skin, muscles, and other parts of your body

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the online service for adverse drug reaction reporting by following the link:

<https://www.sahpra.org.za/Publications/Index/8>.

An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

By reporting side effects, you can help provide more information on the safety of R-CIN PLUS.

5. How to store R-CIN PLUS

Store all medicines out of reach of children.

Store at or below 25 °C in a cool, dry place.

Do not take tablets from the blisters until time for administration.

Keep blisters in the carton until required for use.

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Do not use after the expiry date stated on the carton.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What R-CIN PLUS contains

The active ingredients are rifampicin and isoniazid.

The other ingredients are:

Tablet cores:

Ascorbic acid (anti-oxidant), colloidal silicon dioxide, crospovidone, magnesium stearate, microcrystalline cellulose, pregelatinised starch.

Coating materials:

Hypromellose, colour iron oxide red, polyethylene glycol 4000, simethicone emulsion, talc and titanium dioxide

What R-CIN PLUS looks like and contents of the pack

R-CIN PLUS are brick red coloured, capsule shaped, biconvex film coated tablets with a break-line on one side and plain on the other side.

PVC/PVDC/Aluminium foil blister strips (15) of 6 tablets and (24) of 28 tablets packed into an outer cardboard carton.

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Cold form Aluminium-aluminium foil blister strips of 14 tablets for pack sizes of 56 and 84 packed into an outer carton.

White HDPE container with inner LDPE bag and closed with a white screw cap containing 1 000 tablets.

Holder of Certificate of Registration

Pharma Dynamics (Pty) Ltd

1st Floor, Grapevine House, Steenberg Office Park

Silverwood Close

Westlake, Cape Town

7945, South Africa

Tel: + 27 21 707 7000

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